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WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising a therapeutically effective amount of a Notch protein; and a pharmaceutically acceptable carrier.

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2. The composition of claim 1 in which the Notch protein is a human Notch protein.

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3. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising an amino acid sequence encoded by the DNA sequence depicted in Figure 8A (SEQ ID NO:5), 8B (SEQ ID NO:6), 8C (SEQ ID NO:7), 9A (SEQ ID NO:8), or 9B (SEQ ID NO:9), which is able to be bound by an antibody to a Notch protein; and a pharmaceutically acceptable carrier.

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4. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a Notch amino acid sequence depicted in Figure 8A (SEQ ID NO:5), 8B (SEQ ID NO:6), 8C (SEQ ID NO:7), 9A (SEQ ID NO:8), or 9B (SEQ ID NO:9), which displays one or more functional activities associated with a full-length Notch protein; and a pharmaceutically acceptable carrier.

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5. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a fragment of a human Notch protein consisting essentially of the extracellular domain of the protein; and a pharmaceutically acceptable carrier.

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6. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a region of a Notch protein containing the EGF homologous repeats of the protein; and a pharmaceutically acceptable carrier.

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7. A pharmaceutical composition comprising a therapeutically effective amount of a fragment of a Notch protein lacking a portion of the EGF-homologous repeats of the protein, which fragment is able to be bound by an antibody to a Notch protein; and a pharmaceutically acceptable carrier.

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8. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a functionally active portion of a Notch protein; and a pharmaceutically acceptable carrier.

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9. The composition of claim 8 in which the Notch protein is a human Notch protein.

10. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a functionally active portion of a human Notch protein joined via a peptide bond to a sequence of a protein different from the Notch protein; and a pharmaceutically acceptable carrier.

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11. The composition of claim 10 in which the functionally active portion of the Notch protein is encoded by the human cDNA sequence contained in plasmid hN3k as deposited with the ATCC and assigned accession number 68609, or encoded by the human cDNA sequence contained in plasmid hN5k as deposited with the ATCC and assigned accession number 68611.

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12. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising the amino acid sequence depicted in Figure 10 (SEQ ID NO:11); and a pharmaceutically acceptable carrier.

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13. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising the amino acid sequence

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depicted in Figure 11 (SEQ ID NO:13); and a pharmaceutically acceptable carrier.

5 14. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising the portion of a human Notch protein with the greatest homology to the epidermal growth factor-like repeats 11 and 12 of the *Drosophila* Notch sequence as shown in Figure 4 (SEQ ID NO:14); and a pharmaceutically acceptable carrier.

10 15. A pharmaceutical composition comprising a therapeutically effective amount of a derivative or analog of a Notch protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

15 16. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein; and a pharmaceutically acceptable carrier.

20 17. A pharmaceutical composition comprising a therapeutically effective amount of a fragment of a Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

25 18. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a fragment of a Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta

protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

5 19. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a derivative or analog of a Delta protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

10 20. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a fragment of a Delta protein joined via a peptide bond to a protein sequence of a protein different from the Delta protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch
15 protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

 21. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a derivative or analog of a
20 Serrate protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

 22. A pharmaceutical composition comprising a therapeutically
25 effective amount of a derivative or analog of a Notch protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a second protein expressed on the surface of a second cell, which second protein is selected from the group consisting of a Delta protein and a Serrate protein; and a pharmaceutically acceptable carrier.

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23. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a Notch protein; and a pharmaceutically acceptable carrier.

5 24. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a functionally active portion of a human Notch protein; and a pharmaceutically acceptable carrier.

10 25. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding the amino acid sequence depicted in Figure 10 (SEQ ID NO:11); and a pharmaceutically acceptable carrier.

15 26. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding the amino acid sequence depicted in Figure 11 (SEQ ID NO:13); and a pharmaceutically acceptable carrier.

20 27. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a fragment of a Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

25 28. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a chimeric protein, said chimeric protein comprising a functionally active fragment of a human Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein; and a pharmaceutically acceptable carrier.

30 29. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a fragment of a Delta protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of

a first cell, to bind to a Notch protein expressed on the surface of a second cell;
and a pharmaceutically acceptable carrier.

5 30. A pharmaceutical composition comprising a therapeutically
effective amount of a nucleic acid encoding a fragment of a Serrate protein, which
fragment is characterized by the ability *in vitro*, when expressed on the surface of
a first cell, to bind to a Notch protein expressed on the surface of a second cell;
and a pharmaceutically acceptable carrier.

10 31. The composition of claim 24 in which the nucleic acid is a
nucleic acid vector.

15 32. A pharmaceutical composition comprising a therapeutically
effective amount of an antibody which binds to a Notch protein; and a
pharmaceutically acceptable carrier.

20 33. A pharmaceutical composition comprising a therapeutically
effective amount of a fragment or derivative of an antibody to a Notch protein
containing the idiotype of the antibody; and a pharmaceutically acceptable carrier.

34. A method of treating a disease or disorder in a subject
comprising administering to a subject in need of such treatment a therapeutically
effective amount of a molecule which antagonizes the function of a Notch protein.

25 35. The method according to claim 34 in which the disease or
disorder is a malignancy characterized by increased Notch activity or increased
expression of a Notch protein or of a Notch derivative capable of being bound by
an anti-Notch antibody, relative to said Notch activity or expression in an
analogous non-malignant sample.

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36. The method according to claim 34 in which the disease or disorder is cervical cancer.

5 37. The method according to claim 34 in which the disease or disorder is breast cancer.

38. The method according to claim 34 in which the disease or disorder is colon cancer.

10 39. The method according to claim 35 in which the malignancy is selected from the group consisting of melanoma, seminoma, and lung cancer.

15 40. The method according to claim 35 in which the subject is a human.

41. The method according to claim 36, 37 or 38 in which the molecule is an antibody to Notch or a portion of said antibody containing the binding domain thereof.

20 42. The method according to claim 36, 37 or 38 in which the molecule is a protein consisting of at least the extracellular domain of a Notch protein or a portion thereof capable of binding to a Notch ligand.

25 43. The method according to claim 36, 37 or 38 in which the molecule is a protein consisting of at least the EGF homologous repeats of a Notch protein.

30 44. The method according to claim 36, 37 or 38 in which the molecule is a protein consisting of at least an adhesive fragment of a Notch protein.

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45. The method according to claim 36, 37 or 38 in which the molecule is an oligonucleotide which (a) consists of at least six nucleotides; (b) comprises a sequence complementary to at least a portion of an RNA transcript of a Notch gene; and (c) is hybridizable to the RNA transcript.

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46. A method of treating a disease or disorder in a subject comprising administering to the subject a therapeutically effective amount of a molecule which promotes the function of a Notch protein.

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47. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a Notch protein.

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48. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a functionally active portion of a Notch protein.

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49. The method according to claim 47 in which the Notch protein is a human Notch protein.

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50. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a chimeric protein, said protein comprising a functionally active portion of a Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein.

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51. The method according to claim 49 in which the human Notch protein comprises the amino acid sequence depicted in Figure 10 (SEQ ID NO:11) or Figure 11 (SEQ ID NO:13).

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52. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a derivative or analog of a Notch protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a second protein expressed on the surface of a second cell, which second protein is selected from the group consisting of a Delta protein and a Serrate protein.

53. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a derivative or analog of a Delta protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.

54. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a derivative or analog of a Serrate protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.

55. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a Notch protein.

56. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a functionally active portion of a Notch protein.

57. The method according to claim 55 in which the subject is human and the Notch protein is a human Notch protein.

58. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a fragment of a Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a second protein expressed on the surface of a second cell, which second protein is selected from the group consisting of a Delta protein and a Serrate protein.

59. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a fragment of a Delta protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.

60. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a fragment of a Serrate protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.

61. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of antibody to a Notch protein.

62. The method according to claim 58 in which the antibody is monoclonal.

63. A method for treating a patient with a tumor, of a tumor type characterized by expression of a Notch gene, comprising administering to the patient an effective amount of an oligonucleotide, which oligonucleotide (a) consists of at least six nucleotides; (b) comprises a sequence complementary to at

least a portion of an RNA transcript of the Notch gene; and (c) is hybridizable to the RNA transcript.

5 64. The method according to claim 60 in which the patient is a human, and the Notch gene is a human gene.

 65. An isolated oligonucleotide consisting of at least six nucleotides, and comprising a sequence complementary to at least a portion of an RNA transcript of a Notch gene, which oligonucleotide is hybridizable to the
10 RNA transcript.

 66. A pharmaceutical composition comprising the oligonucleotide of claim 65; and a pharmaceutically acceptable carrier.

15 67. A method of inhibiting the expression of a nucleic acid sequence encoding a Notch protein in a cell comprising providing the cell with an effective amount of the oligonucleotide of claim 65.

 68. A method of diagnosing a disease or disorder characterized by
20 an aberrant level of Notch protein or activity in a patient, comprising measuring the level of Notch protein expression or activity in a sample derived from the patient, in which an increase or decrease in Notch protein or activity in the patient sample relative to the level found in such a sample from a normal individual indicates the presence of the disease or disorder in the patient.
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 69. A method of diagnosing a malignancy characterized by increased Notch activity or increased expression of a Notch protein or of a Notch derivative capable of being bound by an anti-Notch antibody, comprising measuring the level of Notch activity or level of expression of a Notch protein or
30 of a Notch derivative capable of being bound by an anti-Notch antibody, in a sample containing or suspected of containing malignant cells from a patient, in

which an increase in Notch activity or increase in expression of a Notch protein or of a Notch derivative capable of being bound by an anti-Notch antibody, in the sample, relative to said level found in an analogous sample of non-malignant cells indicates the presence of the disease or disorder in the patient.

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70. The method according to claim 69 in which the malignancy is cervical cancer.

10 71. The method according to claim 69 in which the malignancy is breast cancer.

72. The method according to claim 69 in which the malignancy is colon cancer.

15 73. The method according to claim 69 in which the malignancy is selected from the group consisting of melanoma, seminoma, and lung cancer.

20 74. The method according to claim 69 in which the level of expression of the Notch protein or derivative is measured by a method comprising contacting the sample with an anti-Notch antibody such that immunospecific binding can occur, and measuring the amount of any immunospecific binding of the antibody that occurs.

25 75. A method of treating or preventing a nervous system disorder in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a functionally active portion of a Notch protein.

30 76. A method of promoting tissue regeneration or repair in a subject comprising administering to a subject an effective amount of a functionally active portion of a Notch protein.

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77. A method of treating a benign dysproliferative disorder in a subject comprising administering to a subject in need of such treatment an effective amount of a functionally active portion of a Notch protein, in which the disorder is selected from the group consisting of cirrhosis of the liver, psoriasis, keloids, and baldness.

78. A substantially purified human Notch protein comprising the amino acid sequence encoded by the hN homolog as depicted in Figure 13 from amino acid numbers 1 through 2169 (SEQ ID NO:19).

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79. A substantially purified human Notch protein comprising the amino acid sequence encoded by the hN homolog as depicted in Figure 13 from amino acid numbers about 26 through 2169 (as contained in SEQ ID NO:19).

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80. A substantially purified protein comprising the extracellular domain of the mature human Notch protein encoded by the hN homolog, as depicted in Figure 13 from amino acid numbers about 26 through 1677 (as contained in SEQ ID NO:19).

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81. A substantially purified protein comprising the EGF homologous repeats of the mature human Notch protein encoded by the hN homolog, as depicted in Figure 13 from amino acid numbers 26 through 1413 (as contained in SEQ ID NO:19).

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82. A substantially purified protein comprising the EGF like repeats 11 and 12 of the mature human Notch protein encoded by the hN homolog, as depicted in Figure 13 (as contained in SEQ ID NO:19).

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83. A substantially purified protein consisting essentially of the extracellular domain of the mature human Notch protein encoded by the hN

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homolog, as depicted in Figure 13 from amino acid numbers about 26 through 1677 (as contained in SEQ ID NO:19).

5 84. A substantially purified nucleic acid encoding the protein of
claim 78.

85. A substantially purified nucleic acid encoding the protein of
claim 79.

10 86. A substantially purified nucleic acid encoding the protein of
claim 80.

15 87. A substantially purified nucleic acid encoding the protein of
claim 82.

88. The nucleic acid of claim 85 which is a DNA molecule
comprising the sequence depicted in Figure 17 from nucleotide numbers 82
through 7419 (as contained in SEQ ID NO:21).

20 89. The nucleic acid of claim 80 in which the sequence encoding
the extracellular domain is as presented in Figure 17 (as contained in
SEQ ID NO:21).

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